A multicenter study of the application of Six Sigma management in clinical rational drug use via pharmacist intervention

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Aim: The status of outpatient irrational prescription drug use before and after pharmacist interventions in 6 large scale hospitals was investigated to determine the underlying reasons and to promote rational clinical drug use.

Materials and methods: The 5-step DMAIC method (define, measure, analyze, improve, control) in Six Sigma management was utilized to investigate irrational drug use in prescriptions. The statistical software package SAS9.1.3 was adopted to analyze the results, determine possible reasons that could lead to irrational drug use, and then intervene accordingly. Statistics before and after the intervention were compared to analyze the function and effect of Six Sigma management in rational drug use via pharmacist intervention.

Results: Irrational drug use rates (defect rates) before and after the intervention were 8.56% and 4.46% (P < 0.001), the Z value increased from 2.82 to 3.01, and the differences were significant.

Conclusion: Six Sigma management will be able to computerize and refine hospital management, thereby ultimately improving service quality.

Key words: Six Sigma management, outpatient prescription, pharmacist intervention, rational drug use

1. Introduction
The World Health Organization (WHO) defines rational drug use as follows: drugs should be appropriate for the clinical needs of patients, the medicine dosage should meet their individual requirements, the treatment course should be appropriate, and drug prices should be as low as possible for patients and their communities (1). However, the WHO also reports that approximately 30% of patients worldwide die from irrational drug use rather than from the diseases themselves. Irrational drug use delays disease treatment, wastes medical resources, results in adverse drug reactions and drug-induced diseases, and even leads to medical incidents (2–4). Irrational drug use has become a serious problem throughout the world that cannot be ignored, and thus it is imperative to utilize appropriate measures to improve rational drug use levels in the medical institutions in China (5).

Meanwhile, the Chinese government aims to further reinforce the clinical application and management of antibiotics in medical institutions, promote the rational use of antibiotics, effectively control bacterial resistance, and ensure the quality and safety of medical care. To these ends, the Chinese Ministry of Health established the “Specific rectification program for clinical use of antibiotics in 2011”, which was implemented nationwide in July 2011. As a result, the clinical use and management of antibiotics were further reinforced, the clinical use structure of antibiotics was optimized, the clinical drug use level of antibiotics was improved, the clinical use of antibiotics was standardized, and bacterial resistance was effectively suppressed. The outstanding problems therein will be thoroughly solved, which will improve the effective and long-term clinical use of antibiotics as well as facilitate continuous improvement in the future (6,7).

Thus, our department combined Six Sigma management with the program mentioned above to manage clinical drug use through pharmacist intervention, and satisfactory results were obtained (8).
2. Materials and methods

2.1. Sources of statistics
Before the intervention, 18,000 outpatient prescriptions from July to December of 2010 (500 prescriptions per month) were randomly selected in 6 hospitals. Illegible handwriting prescriptions were removed, and the remaining 15,228 prescriptions were included in this study. After the intervention, the same number of outpatient prescriptions from July to December of 2011 were randomly selected, including 17,049 completed prescriptions. The statistics were integral, truthful, and reliable.

2.2. Research methods
The 5-step DMAIC method (define, measure, analyze, improve, control) in Six Sigma management was utilized herein, which was cooperatively carried out by the staff in the Outpatient Pharmacy, the Clinical Pharmaceutical Personnel and Drug Storehouse in the Department of Pharmacy, Medical Affairs, the Information Center, the Evidence-Based Medicine Department, and the Clinical Department in 6 hospitals. The statistical software package SAS9.1.3, brainstorming, and fishbone diagrams were employed (9).

2.2.1. Define
The Six Sigma project team was set up by training the entire staff of the Pharmacy Department in drug instructions, the "Drug Use Notice", "Prescription Management Methods", "Clinical Antibiotics Guidelines", "New Pharmaceutics (16th edition)", "Hospital Prescription Review Management Practices (Trial)", and "Clinical Disease Diagnosis and Treatment Guidelines", which were utilized to evaluate rational drug use (10–13). Irrational prescriptions (defects) were defined as irrational aspects discovered by project leaders that related clinicians and pharmacists did not discern, mainly including inappropriate indication, drug selection, drug formulation, administration route, usage and dosage (inappropriate administration frequency, solvent selection, dosage, and administration time), drug combination, repeated administration, incompatibility, adverse interactions, and medication contraindications. A total of 11 items were tested, each of which was determined to be an irrational use criterion, i.e. a defect. Repeated irrational drug use of one prescription was determined to be one irrational number (defect number). The irrational drug use (defect) examination form was designed before the prescription investigation, yielding the total irrational drug use number (total defect number) (14). Each prescription was utilized as a unit, and the defect opportunity number was equal to the unit number multiplied by the total defect item number. The defect examination form for prescriptions is presented in Table 1.

2.2.2. Measure
Five hundred prescriptions per month from July to December in 2010 were randomly selected in each hospital. Some paper prescriptions suffered from illegible handwriting and missing items. Thus, incomplete prescriptions were removed, and a total of 15,228 prescriptions were incorporated. The total number of prescriptions and the number of irrational drug uses (defect number) were recorded, and the irrational drug use (defect) examination form was filled out. The resulting statistics were collected, and the results are summarized in Table 2. A total of 14,342 defect points were detected based on the following equation: irrational number per 1,000,000 opportunities (defect number) = total irrational number (defect number) at each check point/(irrational number per unit × total unit number) × 106. The irrational item number per unit was 11. The total unit number, i.e. the total number of sampled prescriptions, was 15,228. The irrational number (defect number) per 1,000,000 opportunities = 14,342/(11 × 15,228) × 106 = 85,619.79, and the defect rate was 8.56%. The statistical software package Minitab15 was utilized to calculate the process capability Z value as 2.82.

<table>
<thead>
<tr>
<th>Defect item</th>
<th>Defect attribution and number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate indication</td>
<td>An irrational drug = a defect point</td>
</tr>
<tr>
<td>Inappropriate drug selection</td>
<td>An irrational drug = a defect point</td>
</tr>
<tr>
<td>Inappropriate drug formulation and administration route</td>
<td>An irrational drug = a defect point</td>
</tr>
<tr>
<td>Inappropriate administration frequency</td>
<td>An irrational drug = a defect point</td>
</tr>
<tr>
<td>Inappropriate solvent selection</td>
<td>An irrational drug = a defect point</td>
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<tr>
<td>Inappropriate dosage</td>
<td>An irrational drug = a defect point</td>
</tr>
<tr>
<td>Inappropriate administration time</td>
<td>An irrational drug = a defect point</td>
</tr>
<tr>
<td>Inappropriate drug combination</td>
<td>An irrational drug combination = a defect point</td>
</tr>
<tr>
<td>With incompatibility and adverse interaction</td>
<td>An incompatibility or an adverse interaction = a defect point</td>
</tr>
<tr>
<td>Medication contraindication</td>
<td>A medication contraindication = a defect point</td>
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</table>
As shown in Table 2, irrational administration frequency, at 4687, was the most significant item, followed by irrational administration dosage at 4168.

2.2.3. Analyze

All the staff were convened for brainstorming, which was combined with the statistical results of prescriptions and rational drug use questionnaires administered to clinicians, nurses, and patients. The main reasons leading to irrational drug use were determined in order to plot a fishbone diagram (Figure) for analysis (15).

2.2.4. Improve

This stage aims to ensure that the proposed method can meet or exceed the target. Solutions were found for the causes of irrational drug use listed in the fishbone diagram. The same basic measures were utilized by each hospital, which are summarized as follows.

Hospital websites, billboards, knowledge competitions, etc., were utilized to inform and train the staff in the guidelines mentioned in the Section "Define". Lectures and training sessions concerning rational drug use were also conducted regularly. A series of measures, including a rational drug use management system, a clinical use and monitoring system for antibiotics, preventive use principles for perioperative antibiotics, a warning system for abnormal antibiotics, elimination of the successive top 10 clinicians who prescribed antibiotics, and hospital prescription review management practices, were implemented to clarify the authorities of all-level clinicians for a variety of antibiotics for prevention and treatment (16,17).

Administration route and time were also regulated in detail. A basic hospital medication catalog, a hospital drug formulary, and a hospital drug specification summary were developed. Drug communications were published regularly to inform the medical staff of the latest drug information, drug policies, laws, and regulations (18). Medical ethics education was carried out to make the medical staff fully aware of the importance of emotional, humane, and psychological services, which will enhance their responsibility and commitment to acquire the trust and understanding of patients and to establish a good rapport with them.

A prescription intervention and review group consisting of multi-disciplinary experts was set up to randomly check the outpatient prescriptions monthly and post the results on hospital websites. Prescription review results were included in the performance appraisal and annual assessment of the relevant departments and staff therein. Clinicians who had prescribed irrational prescriptions more than once without compelling reasons were warned and their authority restricted. More than one subsequent abnormal prescription would lead to cancellation of the clinician’s prescribing authority. In addition, clinicians who failed computer operation tests were deprived of their prescribing authority. Each instance of irrational drug use owing to improper computer operations (dosage errors, incorrect typing of oral and external drugs instead of intravenous injection and oral drugs, etc.) was punished monetarily. The hospital information system (HIS) was continuously improved: special drug usages (e.g., blood purification, skin tests, preprandial and postprandial drugs) were added to the usage option (19). Meanwhile, doctor input function was also added to enhance the flexibility of the program. Infusion prescriptions were
normalized such that they are to be prescribed according to the actual administration groups for the convenient review of pharmacists.

All departments were assigned adverse drug reaction liaisons who were trained regularly and were responsible for monitoring, submitting, and reporting adverse drug reactions in their own departments.

The Nursing Department cooperatively counted and summarized the common dosage, usage, incompatibility, and other factors of common drugs in each department. Nurses who were aware of the distributed summarizations were tested, and those found to be unqualified were punished monetarily and required to participate in supplementary examinations.

On the basis of the actual situation, the functions of clinical pharmacists were defined as servicing and consulting. On one hand, pharmacists should provide clinical references for pharmacokinetics, pharmacoeconomics, pharmacoepidemiology, pharmaceutics, adverse drug reactions, and drug interactions on a weekly basis, and they should also report the clinical treatment requirements in a timely fashion. On the other hand, medication consultation services were specifically set up in the outpatient pharmacy to receive outpatient medication consultations and guide the patients with rational drug use information (20,21).

Abnormal sales of drugs were monitored in time by reporting the top 10 sales of common drugs and antibiotics. In addition, the top-selling antibiotics were eliminated quarterly to effectively strengthen hospital infection control and to resist illegal promotion of pharmaceutical suppliers. Pharmacists underwent regular professional training to improve their ability to handle possible problems and to foster timely cooperation with clinicians. Moreover, irrational drug use prescriptions were registered, summarized, and analyzed to prevent similar incidents, improve drug use levels, and minimize the occurrence of irrational drug use.

Workflow was optimized by adding a prescription review function by pharmacists to the HIS. Full-time clinical pharmacists in the Pharmacy Department were utilized to review the prescriptions issued by clinicians, whereas the dispensing pharmacists were only in charge of dispensing drugs and guiding administration. As a result, prescription review pharmacists and dispensing pharmacists became more specialized, which increased the efficiency of the former and reduced the workload of the latter, significantly reducing irrational drug use.

A standard operation procedure was developed to standardize and systematize drug use guidance. Meanwhile, each drug was tagged with the usage and dosage, and special notices.

The working effect was added to the performance appraisal system to investigate the patients. The mark rate and the accuracy of drug usage, dosage, and notice were incorporated. Various forms of publicity and education concerning rational drug use were carried out. Frequently asked questions were summarized and then printed in brochures, which were distributed to patients for free.

Pharmacists initially exchanged contact details with chronically ill, elderly, and combination therapy patients in order to provide consultation at any time. The patients were contacted regularly to assess the drug use situation and provide guidance accordingly (22).

2.2.5. Control

Based on the improve stage, this stage emphasizes the development of control measures by the Department of Pharmacy to coordinate with other relevant departments in order to evaluate the improvement effects, and to summarize and solve possible problems in time to ensure
3. Results
The control stage lasted for 6 months until basic stability was achieved. Every month from July to December in 2011, 500 prescriptions were randomly selected in each hospital. The total number of prescriptions was 17,049, which covered all departments in the hospitals. The drug use conditions in the prescriptions were investigated, and the defect rate was 4.46%, which was 4.11% lower than the rate prior to the intervention (Table 2). The Z value was 3.01, an increase of 0.19 compared to that before the intervention. On the t-test, P < 0.01.

4. Discussion
As a special service agency, the hospital plays a direct role in human health that is in need of much higher quality standards than other fields (24). The medical service has also transformed to the mode that centralizes quality management from the needs to the satisfaction of patients, which determines the profit and development of hospitals. Owing to the continuous development of medical science and technology, more specialized third divisions, more examination techniques, accelerated daily life, and increased outpatients, it is imperative to improve value-added service quality and patient satisfaction, significantly reduce the limitation time on people, goods, and equipment, and job switching time, simplify non-value-added behaviors and processes in inventory, and eventually lower operating costs. Therefore, hospital administrators should introduce excellent enterprise management methods to increase comprehensive competitiveness (25).

Six Sigma (6σ) is a target indicating that 99,999.96% of all processes and results are defect-free. In other words, only 4 things are allowed to be defective out of 1,000,000 things performed. As a quality management concept, Six Sigma was first proposed by Bill Smith in Motorola in 1986. This method has been verified to be effective in numerous transnational corporations such as General Electric, Dell, HP, Siemens, and Sony. After being introduced in China in the late 1990s, the Six Sigma management method was initially applied to manufacturing and logistics, which began to be used in hospital management after 1999 (26,27).

Six Sigma management essentially consists of a process improvement model, DMAIC: define, measure, analyze, improve, and control. This method focuses on customer needs, depends greatly on statistical data, emphasizes the improvement of workflow, carries out initiative management, and encourages enterprise culture characteristics such as cooperation without boundaries and diligent learning (28,29). In addition, this method is advantageous in terms of enhanced enterprise management, economized operating costs, elevated customer value, improved service levels, and positive enterprise culture.

Applying the Six Sigma management concept to the clinical use of antibiotics in order to improve the rational drug use level and guarantee medical safety is a long-term task that is in need of constantly improved management and working systems along with working methods. With the further development of a specific rectification program for antibiotics in China, the corresponding clinical use management of antibiotics and other related systems is gradually being established and improved (30). As a result, clinical use management of antibiotics is gradually becoming institutionalized and standardized, and the resulting long-term working mechanism will be able to promote the continuous improvement of antibiotics in clinical application (31).

We applied advanced Six Sigma management in order to intervene in clinical drug use via pharmacists, cultivate administrators, doctors, nurses, and staff in pharmacies and drug stores, optimize hospital processes, and ultimately improve service quality. However, irrational drug use is a comprehensive issue related to concept, habit, technology, and management, leading to the involvement of government agencies, health sectors, drug administration sectors, pharmaceutical sales sectors, news agencies, and hospital management sectors, and not merely clinicians, pharmacists, nurses, and patients.

References


